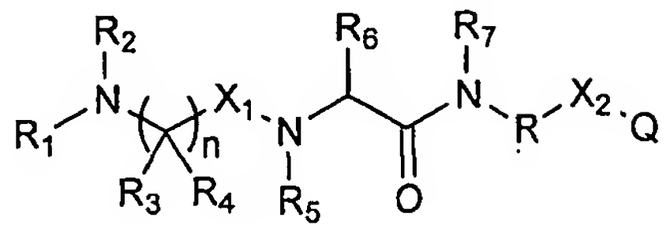
CLAIMS

What is claimed is:

1. A compound having the structure **(I)**:



(I)

and pharmaceutically acceptable derivatives thereof;

wherein n is 0, 1, 2, 3 or 4;

$\mathbf{X_1}$ and $\mathbf{X_2}$ are each independently CR_AR_B, C(=O), or $-SO_2-$; wherein each occurrence of R_A and R_B is independently hydrogen, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

$\mathbf{R_1}$ and $\mathbf{R_2}$ are each independently hydrogen, $-(C=O)R_C$ or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein each occurrence of R_C is independently hydrogen, OH, OR_D, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein R_D is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of $\mathbf{R_3}$ and $\mathbf{R_4}$ is independently hydrogen, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; or wherein any two R_1, R_2, R_3 and R_4 groups, taken together, may form an alicyclic, heteroalicyclic, alicyclicc(aryl), heteroalicyclic(aryl), alicyclic(heteroaryl) or heteroalicyclic(heteroaryl) moiety, or an aryl or heteroaryl moiety;

$\mathbf{R_5}$, $\mathbf{R_6}$ and $\mathbf{R_7}$ are each independently hydrogen, $-(C=O)R_E$ or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_E is independently hydrogen, OH, OR_F, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or wherein any two R_5, R_6 and R_7 groups, taken together, form an alicyclic, heteroalicyclic, alicyclic(aryl), heteroalicyclic(aryl), alicyclic(heteroaryl) or heteroalicyclic(heteroaryl) moiety, or an aryl or heteroaryl moiety; wherein R_F is an aliphatic, alicyclic, heteroaliphatic,

heteroalicyclic, aryl or heteroaryl moiety; or R_7 may be absent when NR_7 is linked to R via a double bond;

R is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

Q is $OR^{Q'}$, $SR^{Q'}$, $NR^{Q'}R^{Q''}$, N_3, =N-OH, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein $R^{Q'}$ and $R^{Q''}$ are each independently hydrogen, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or $R^{Q'}$ and $R^{Q''}$, taken together with the nitrogen atom to which they are attached, may form an alicyclic, heteroalicyclic, alicyclic(aryl), heteroalicyclic(aryl), alicyclic(heteroaryl) or heteroalicyclic(heteroaryl) moiety, or an aryl or heteroaryl moiety;

with the proviso that:

(viii) the compound is not a naturally occurring Hemiasterlin; and

(ix) the following groups do not occur simultaneously as defined:

n is 1;

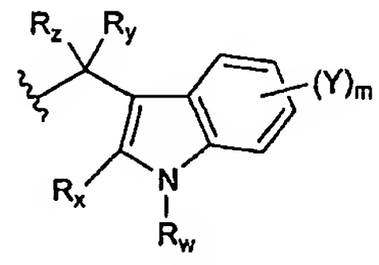
X_1 and X_2 are each C(=O);

R_1 is hydrogen, an optionally substituted alkyl or acyl group, or an optionally substituted methylene or –CH= group bonded to the indole moiety thereby forming a tricyclic moiety;

R_2 is hydrogen, an optionally substituted alkyl or acyl group, or is absent when R_1 is –CH= as defined above;

R_3 is hydrogen or is absent when CR_3 and CR_yR_z, as defined herein, are linked by a double bond;

R_4 is a moiety having the structure:



wherein R_w, R_y and R_z are each independently hydrogen, or optionally substituted alkyl or acyl, or R_z is absent when CR_3 and CR_yR_z, as defined herein, are linked by a double bond; with the limitation that R_y and R_z are not simultaneously hydrogen; R_x is hydrogen or an optional

substituent, or is absent when R_1 is an optionally substituted methylene or –CH= group as defined above; Y is an optional substituent; and m is 0, 1, 2, 3 or 4;

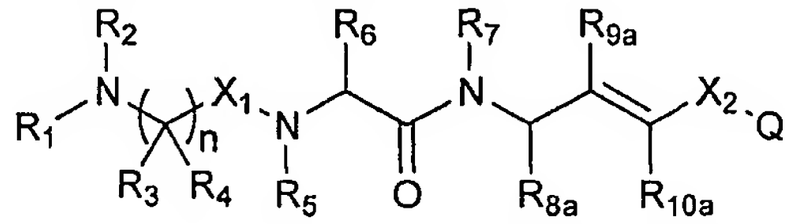
R_5 is hydrogen, OH or an optionally substituted alkyl or acyl group;

R_6 is hydrogen or an optionally substituted alkyl group;

R_7 is hydrogen or alkyl; and

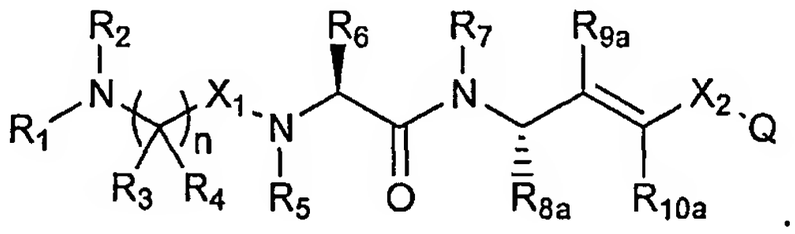
–R-X_2-Q together represent an optionally substituted alkyl moiety or –Q′-C(O)X, wherein Q′ is an optionally substituted –CH_2-, -CH_2CH_2-, -$CH_2CH_2CH_2$-, -CH_2CH=CH-, -CH_2C=-C- or phenylene moiety, wherein X is –OR′, -SR′ or –NR′R″ and each occurrence of R′ and R″ is independently hydrogen or optionally substituted alkyl.

2. The compound of claim 1 wherein R is –CH(R_{8a})C(R_{9a})=C(R_{10a})- and the compound has the following structure:

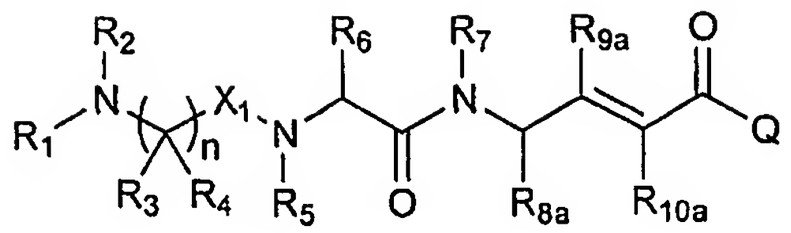


wherein R_{8a}, R_{9a} and R_{10a} are each independently hydrogen, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and wherein any two R_7, R_{8a}, R_{9a} and R_{10a} groups may form an alicyclic, heteroalicyclic, alicyclicc(aryl), heteroalicyclic(aryl), alicyclic(heteroaryl) or heteroalicyclic(heteroaryl) moiety, or an aryl or heteroaryl moiety.

3. The compound of claim 2 having the following stereochemistry:

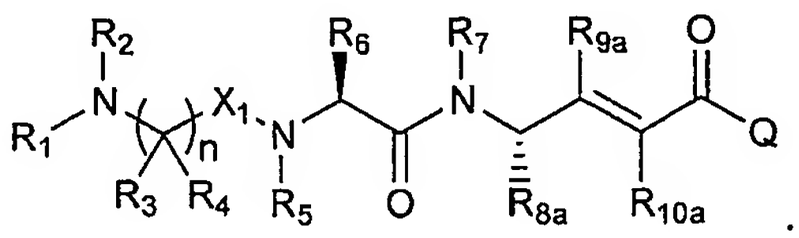


4. The compound of claim 2 wherein X_2 is C=O and the compound has the following structure:

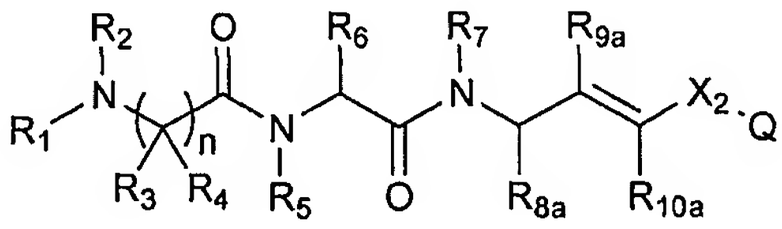


wherein X_1 is C=O, SO_2, or CR_AR_B, wherein R_A and R_B are each independently hydrogen, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety.

5. The compound of claim 4 having the following stereochemistry:

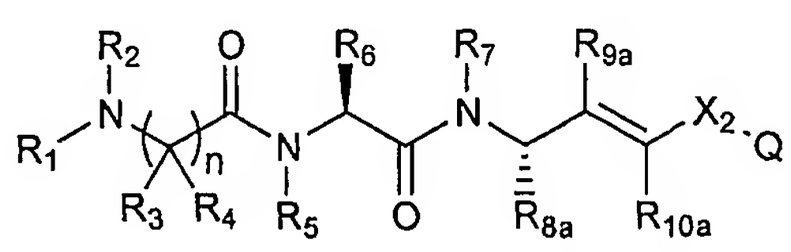


6. The compound of claim 2 wherein X_1 is C=O and the compound has the following structure:

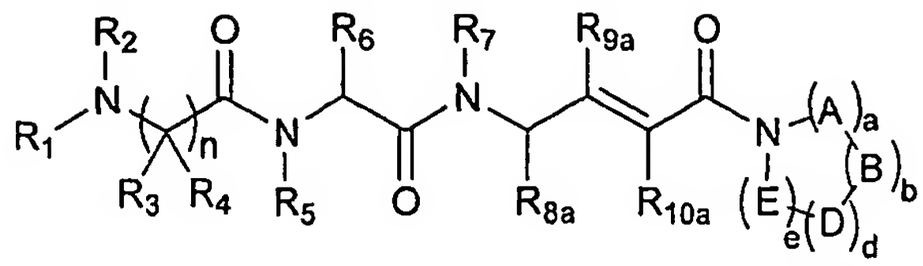


wherein X_2 is C=O, SO_2, or CR_AR_B, wherein R_A and R_B are each independently hydrogen, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety.

7. The compound of claim 6 having the following stereochemistry:



8. The compound of claim 4 wherein X_1 is C=O; Q is an optionally substituted nitrogen-containing cyclic moiety; and the compound has the following structure:

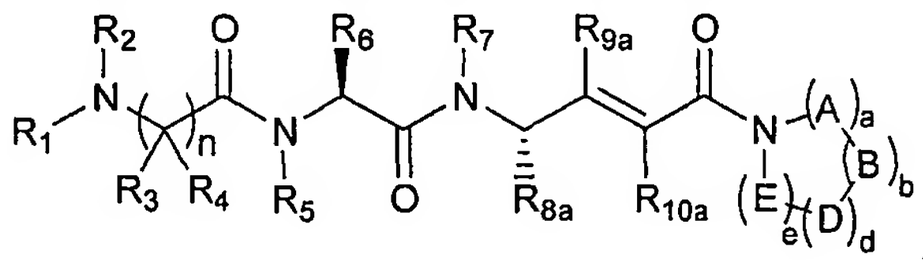


wherein each occurrence of A, B, D or E is independently CHR^i, CR^iR^{ii}, O, S, NR^iR^{ii}, wherein each occurrence of R^i and R^{ii} is independently absent, hydrogen, $-C(=O)R^{iii}$, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; or wherein any two adjacent R^i, R^{ii} or R^{iii} groups, taken together, form a alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety; wherein each occurrence of R^{iii} is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

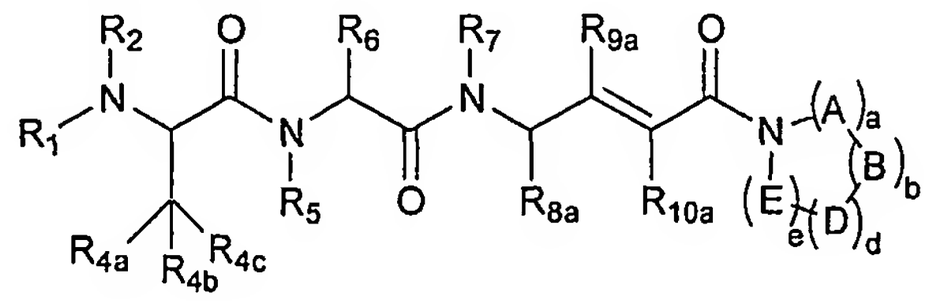
N and A, A and B, B and D, D and E, and E and N are each independently linked by a single or double bond as valency permits; and

a, b, d and e are each independently 0, 1, 2, 3, 4, 5, 6 or 7, wherein the sum of a, b, d and e is 4-7.

9. The compound of claim 8 having the following stereochemistry:



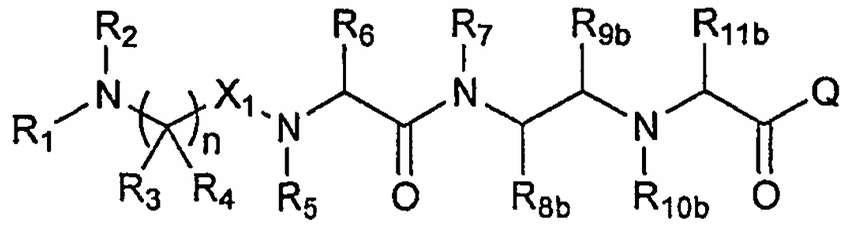
10. The compound of claim 8 wherein n is 1; R_1 and R_2 are each independently hydrogen or methyl; R_3 is hydrogen and R_4 is $-CR_{4a}R_{4b}R_{4c}$; and the compound has the structure:



wherein R_{4a} and R_{4b} are each independently hydrogen or lower alkyl and R_{4c} is an aryl or heteroaryl moiety.

11. The compound of claim 10 wherein R_{4c} is substituted or unsubstituted phenyl.

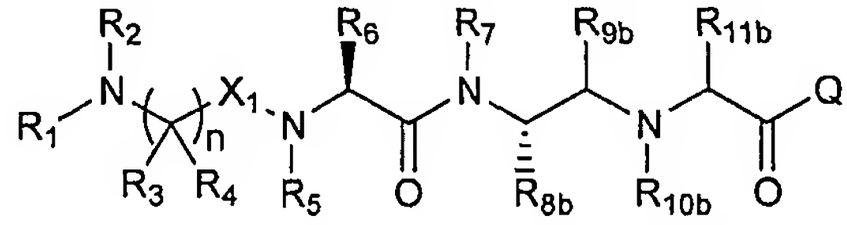
12. The compound of claim 1 having the following structure:



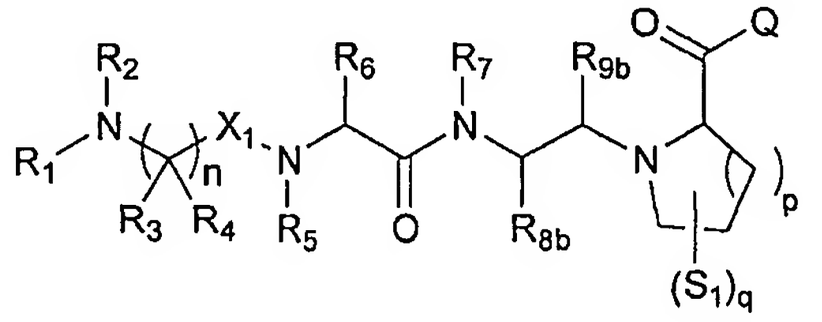
wherein R_{8b}, R_{9b}, R_{10b} and R_{11b} are each independently absent, hydrogen, -(C=O)R_L or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_L is independently hydrogen, OH, OR_M, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or wherein any two R_{8b}, R_{9b}, R_{10b} and R_{11b} groups, taken together, form a alicyclic or heteroalicyclic moiety, or an aryl or heteroaryl moiety; wherein R_M is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

NR_7 and CR_{8b}, CR_{8b} and CR_{9b}, CR_{9b} and CR_{10b}, CR_{10b} and CR_{11b} are each independently linked by a single or double bond as valency permits.

13. The compound of claim 12 having the following stereochemistry:



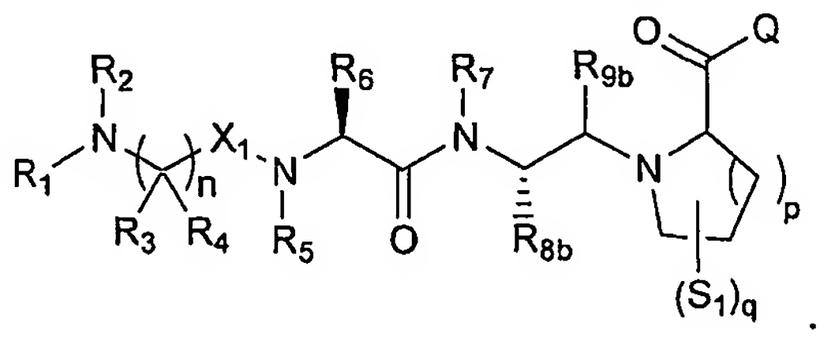
14. The compound of claim 1 having the structure:



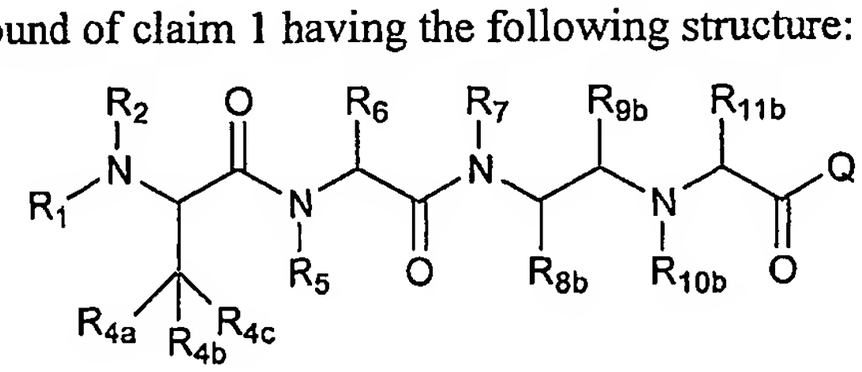
wherein p is 1, 2, 3 or 4; q is 0-12; and each occurrence of S_1 is independently an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or any two adjacent S_1 moieties, taken together, may form an an alicyclic, heteroalicyclic, aryl or heteroaryl moiety.

15. The compound of claim 14 wherein p is 1 and q is 0.

16. The compound of claim 14 having the following sterochemistry:



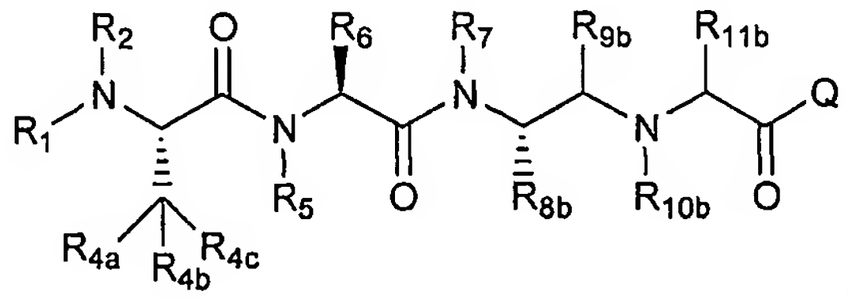
17. The compound of claim 1 having the following structure:



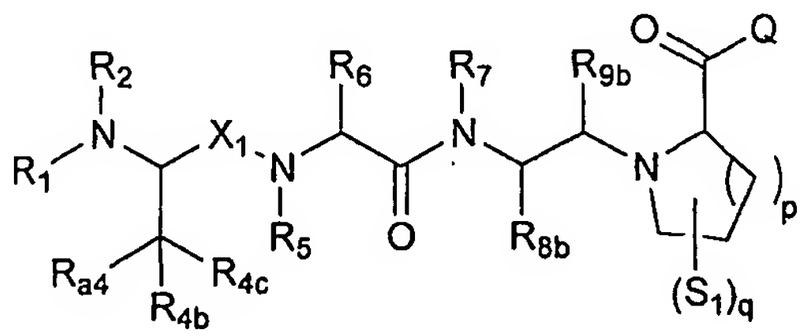
wherein R_{4a} and R_{4b} are each independently lower alkyl and R_{4c} is an aryl or heteroaryl moiety.

18. The compound of claim 17 wherein R_{4c} is substituted or unsubstituted phenyl.

19. The compound of claim 17 wherein the compound has the following structure:

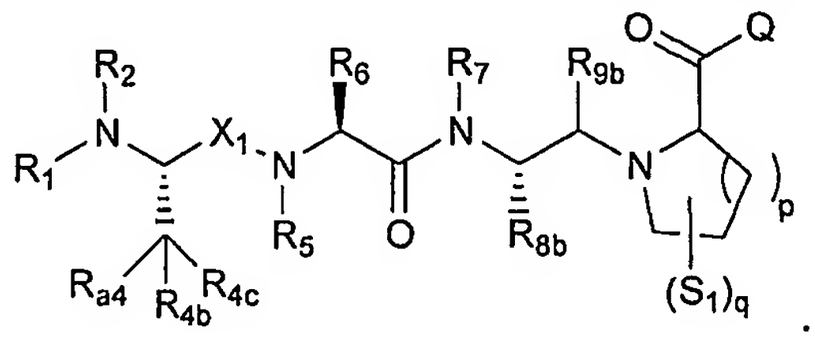


20. The compound of claim 1 having the structure:

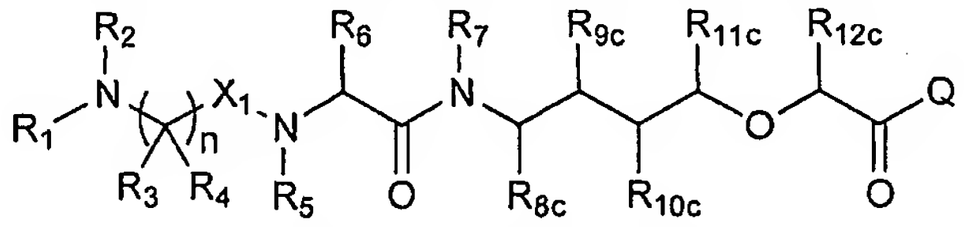


wherein p is 1, 2, 3 or 4; q is 0-12; and each occurrence of S_1 is independently an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or any two adjacent S_1 moieties, taken together, may form an alicyclic, heteroalicyclic, aryl or heteroaryl moiety.

21. The compound of claim 20 having the following sterochemistry:



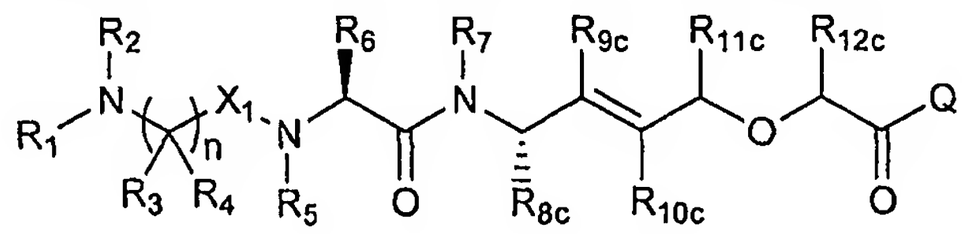
22. The compound of claim 1 having the following structure:



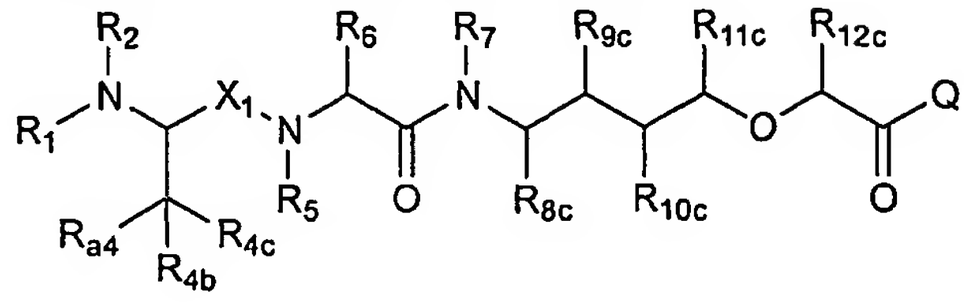
wherein R_{8c}, R_{9c}, R_{10c}, R_{11c} and R_{12c} are each independently hydrogen, -(C=O)R_L or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_L is independently hydrogen, OH, OR_M, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or wherein any two R_{8c}, R_{9c}, R_{10c}, R_{11c} and R_{12c} groups, taken together, form a alicyclic or heteroalicyclic moiety, or an aryl or heteroaryl moiety; wherein R_M is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

NR_7 and CR_{8c}, CR_{8c} and CR_{9c}, CR_{9c} and CR_{10c}, and CR_{10c} and CR_{11c} are each independently linked by a single or double bond as valency permits.

23. The compound of claim 22 having the following structure:



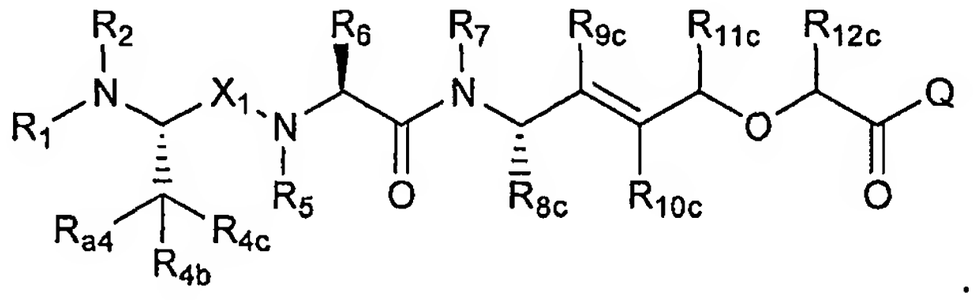
24. The compound of claim 1 having the structure:



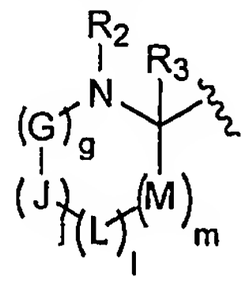
wherein R_{4a} and R_{4b} are each independently lower alkyl and R_{4c} is a substituted or unsubstituted aryl or heteroaryl moiety.

25. The compound of claim 24 wherein R_{4c} is substituted or unsubstituted phenyl.

26. The compound of claim 24 wherein the compound has the following structure:



27. The compound any one of claims 1, 2, 4, 6, 8, 12, 14 and 22, wherein the moiety $-(CR_3R_4)_nNR_1R_2$ has the following structure:



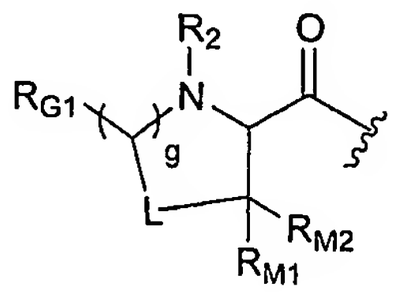
wherein R_3 is hydrogen or is absent when the carbon atom bearing R_3 is linked to N or M via a double bond, and each occurrence of G, J, L and M is independently CHR^{iv}, $CR^{iv}R^{v}$, O, S, $NR^{iv}R^{v}$, wherein each occurrence of R^{iv} and R^{v} is independently absent, hydrogen, $-C(=O)R^{vi}$, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; or wherein any two adjacent R_2, R^{iv}, R^{v} or R^{vi} groups, taken together, form a alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety; wherein each

occurrence of R^{vi} is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

N and G, G and J, J and L, L and M, M and CR_3, and CR_3 and N are each independently linked by a single or double bond as valency permits; and

g, j, l and m are each independently 0, 1, 2, 3, 4, 5 or 6, wherein the sum of g, j, l and m is 3-6.

28. The compound of claim 27 wherein j is 0; l and m are each 1; R_3 is hydrogen; G is CR_{G1}; M is $CR_{M1}R_{M2}$, and the moiety $-X_1-(CR_3R_4)_nNR_1R_2$ has the following structure:



wherein g is 1, 2, 3 or 4;

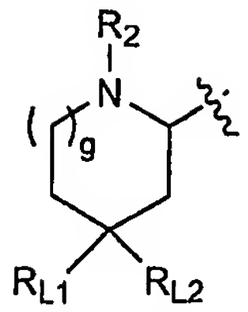
L is $CR_{L1}R_{L2}$, S, O or NR_{L3}, wherein each occurrence of R_{L1}, R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1}, R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1}, R_{L2}, R_{L3}, R_{G1}, R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

29. The compound of claim 28 wherein R_2 is hydrogen, lower alkyl or acyl; R_{G1} is hydrogen, lower alkyl or phenyl; and R_{M1} and R_{M2} are each independently hydrogen, lower alkyl, phenyl or R_{M2} is absent when R_{M1}, taken together with a substituent on L, forms an aryl or heteroaryl moiety.

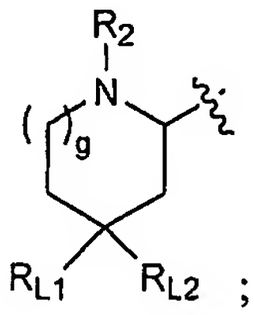
30. The compound of claim 27 wherein G, J and M are each CH_2; j, l and m are each 1; and the moiety $-(CR_3R_4)_nNR_1R_2$ has the following structure:



wherein R_{L1} and R_{L2} are each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety.

31. The compound of claim 30 wherein R_2 is hydrogen, lower alkyl or acyl; R_{L1} and R_{L2} are each independently hydrogen, lower alkyl, heteroalkyl, aryl or heteroaryl.

32. The compound of claim 4 or 6 wherein the moiety $-(CR_3R_4)_nNR_1R_2$ has the following structure:



wherein g is 1, 2, 3 or 4;

R_{L1} and R_{L2} are each independently hydrogen, lower alkyl, heteroalkyl, aryl or heteroaryl;

R_2 is hydrogen, lower alkyl or acyl;

R_5 and R_{9a} are each hydrogen;

R_6 is *tert*-butyl;

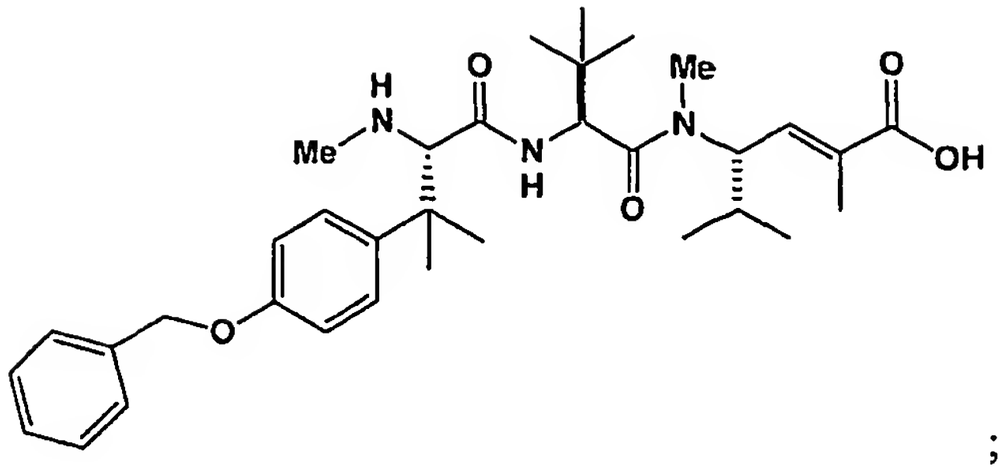
R_7 is methyl;

R_{8a} is *iso*-propyl;

R_{10a} is lower alkyl; and

Q is $OR^{Q'}$ or $NR^{Q'}R^{Q''}$, wherein $R^{Q'}$ and $R^{Q''}$ are each independently hydrogen, lower alkyl, heteroalkyl, aryl or heteroaryl, or wherein $R^{Q'}$ and $R^{Q''}$, taken together with the nitrogen atom to which they are attached, form a heterocyclic or heteroaryl moiety.

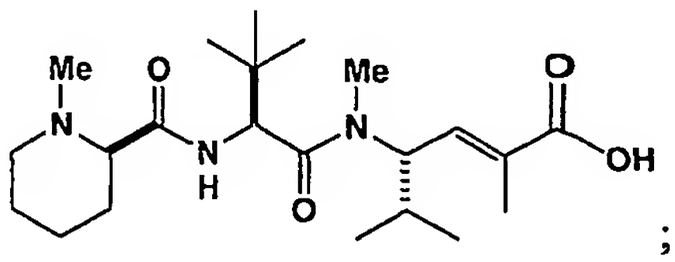
33. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

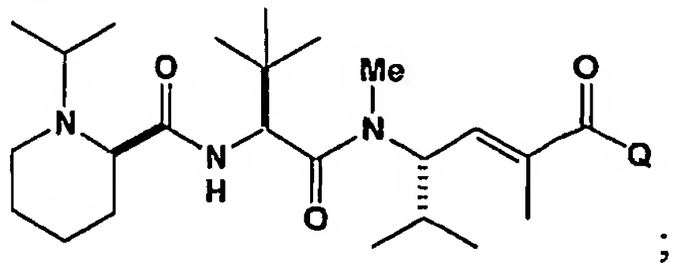
34. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

35. The compound of claim 1 having the structure:

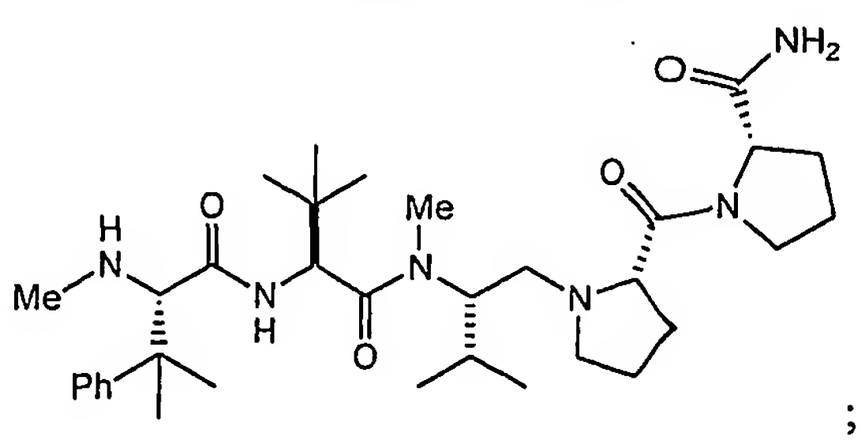


;

wherein Q is OH or Et;

or a pharmaceutically acceptable salt thereof.

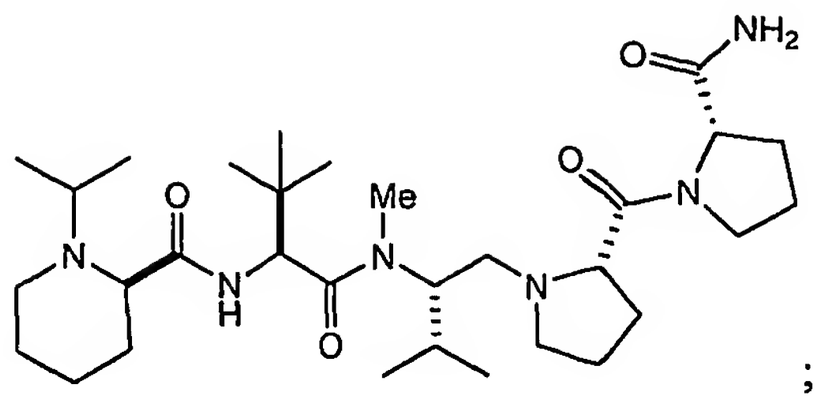
36. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

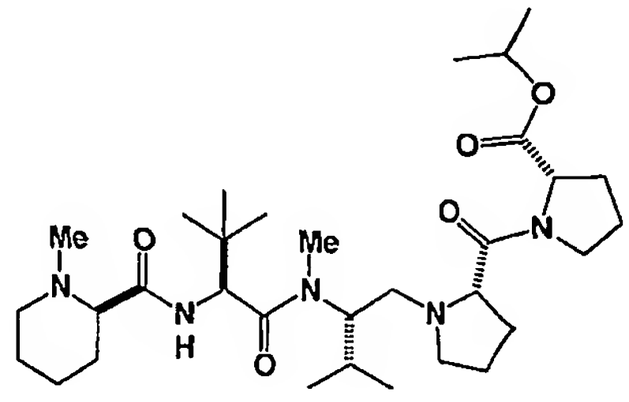
37. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

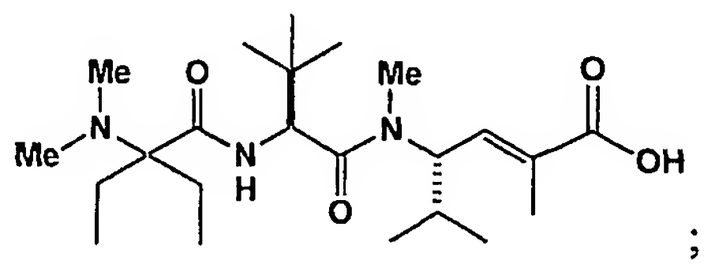
38. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

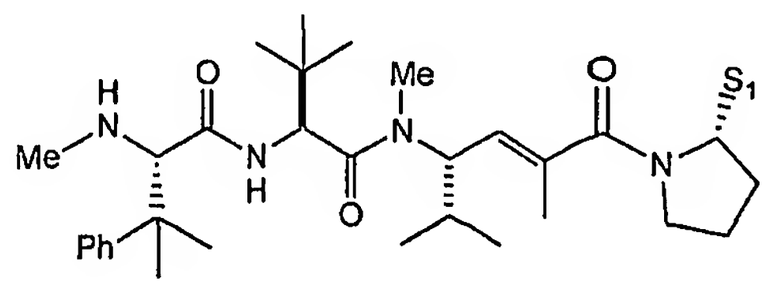
39. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

40. The compound of claim 1 having the structure:

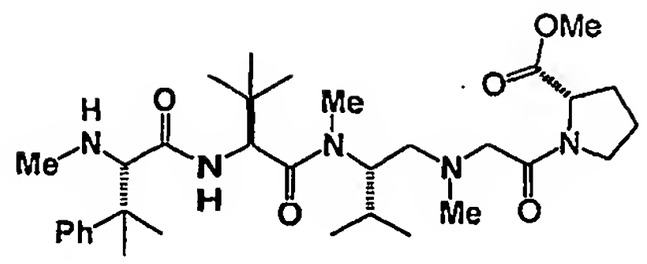


;

wherein S_1 is H, -CH_2OMe, -C(=O)OMe or –$C(=O)NH_2$;

or a pharmaceutically acceptable salt thereof.

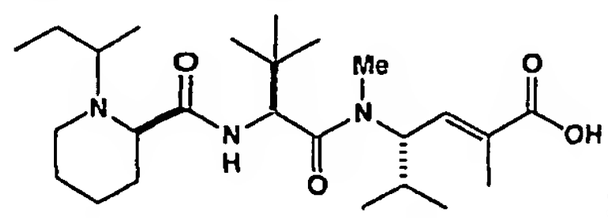
41. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

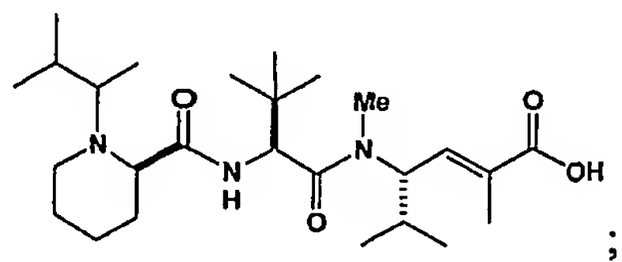
42. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

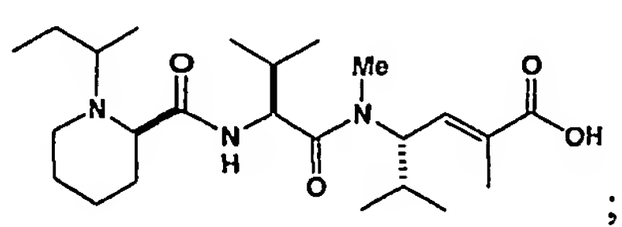
43. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

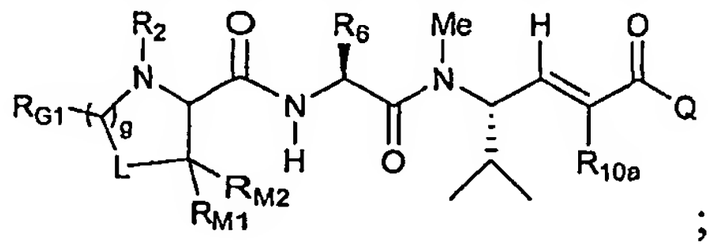
44. The compound of claim 1 having the structure:



;

or a pharmaceutically acceptable salt thereof.

45. An intermediate for the preparation of a compound having the structure:



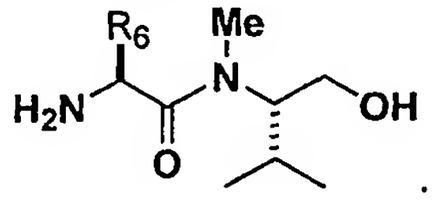
;

wherein g is 1, 2, 3 or 4;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3}, wherein each occurrence of R_{L1}, R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

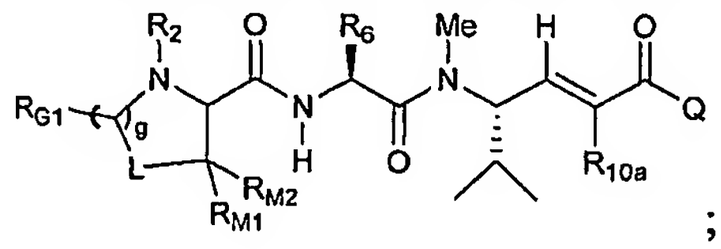
each occurrence of R_{G1}, R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and wherein any two adjacent R_{L1}, R_{L2}, R_{L3}, R_{G1}, R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety; and

wherein said intermediate has the following structure:



.

46. An intermediate for the preparation of a compound having the structure:



;

wherein g is 1, 2, 3 or 4;

R_2 is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety;

R_6 is substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

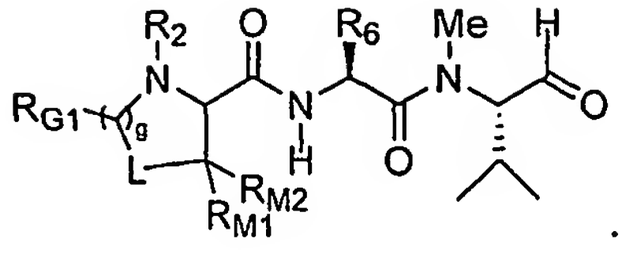
R_{10a} is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3}, wherein each occurrence of R_{L1}, R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1}, R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1}, R_{L2}, R_{L3}, R_{G1}, R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety; and

wherein said intermediate has the following structure:



47. The intermediate of claim 46 wherein R_2 is substituted or unsusbtituted, linear or branched, cyclic or acyclic, saturated or unsaturated lower alkyl.

48. The intermediate of claim 46 wherein R_2 is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -$CH(CH_3)Et$, -$CH(CH_3)CH_2CH_2CH_3$, -$CH_2CH(CH_3)_2$, -$CH(CH_3)CH(CH_3)_2$, -$C(CH_3)_2Et$, -$CH(CH_3)$cyclobutyl, -$CH(Et)_2$, -$C(CH_3)_2C{\equiv}CH$, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.

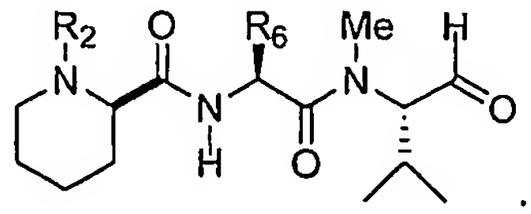
49. The intermediate of claim 46 wherein R_2 is hydrogen, methyl or benzyl.

50. The intermediate of claim 46 wherein R_2 is hydrogen or methyl.

51. The intermediate of claim 46 wherein R_6 is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -$CH(CH_3)CH_2CH_3$, -$CH_2CH(CH_3)_2$, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.

52. The intermediate of claim 46 wherein R_6 is *tert*-butyl.

53. The intermediate of claim 46 having the structure:



54. The intermediate of claim 46 wherein R_6 is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -$CH(CH_3)CH_2CH_3$, -$CH_2CH(CH_3)_2$, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl; and R_2 is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -$CH(CH_3)Et$, -$CH(CH_3)CH_2CH_2CH_3$, -

$CH(CH_3)CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)CH(CH_3)_2$, $-C(CH_3)_2Et$, $-CH(CH_3)$cyclobutyl, $-CH(Et)_2$, $-C(CH_3)_2C{\equiv}CH$, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.

55. A pharmaceutical composition comprising a compound of claim 1, a pharmaceutically acceptable carrier or diluent, and optionally further comprising an additional therapeutic agent.

56. The pharmaceutical composition of claim 55 wherein the compound is present in an amount effective to inhibit cancer cell growth *in vitro*.

57. The pharmaceutical composition of claim 55 wherein the compound is present in an amount effective to cause tumor regression *in vivo*.

58. A method for treating cancer comprising:

administering to a subject in need thereof a therapeutically effective amount of a compound of claim 1, and a pharmaceutically acceptable carrier or diluent, and optionally an additional therapeutic agent.

59. The method of claim 58, wherein the method is used to treat prostate, breast, colon, bladder, cervical, skin, testicular, kidney, ovarian, stomach, brain, liver, pancreatic or esophageal cancer or lymphoma, leukemia, or multiple myeloma.

60. The method of claim 59, wherein the cancer is a solid tumor.

61. The method of claim 59, wherein the cancer is a non-solid tumor.